CLINICO-PATHOLOGICAL STUDY OF SKIN SURFACE EPIDERMAL AND APPENDAGEAL TUMOURS

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CERTIFICATE

This is to certify that this Dissertation entitled **"CLINICO-PATHOLOGICAL STUDY OF SKIN SURFACE EPIDERMAL AND APPENDAGEAL TUMOURS**" is a bonafide work done by **DR.G.BALAJI,** Postgraduate student of Department of Dermatology, Leprosy and Institute of STD, Madras Medical College and Government General Hospital, Chennai – 3 for the award of Degree of M.D.(Dermatology, Venereology and Leprosy) Branch XII – A during the academic year of 2003-2006. This work has not previously formed in the basis for the award of any degree or diploma.

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CONTENTS

INTRODUCTION

Tumours of epidermis are histopathologically diverse group of entities which have in common a localized proliferation of keratinocytes resulting in clinically discrete lesions. They may be divided into a number of categories, reflecting their different biological behaviour.These includes hamartomas, benign tumours, premalignant and malignant conditions.

The cutaneous appendages give rise to a bewildering number of neoplasms (more than eighty in number).Various classification have been proposed in the past which have required modifications from time to time in the light of most recent ultra structural, histochemical findings and the reporting of new morphological entities.

This study of tumours of epidermis and appendages has been undertaken to find out the frequency of benign and malignant growths. The study has been limited to the cases attending the Dermatology Department, Government General Hospital, Chennai.

Most of the tumours whether benign or malignant are symptom less but are cosmetically unacceptable.

This study is based on the classification of tumours given in the LEVERS histopathology of skin 8th edition and is confined to the tumours of epidermis and appendages.

REVIEW OF LITERATURE

More than 100years ago, the noted pathologist Rudolph Virchow portrayed the skin as a protective covering for more delicate and functionally sophisticated internal viscera [(1)]

During the past three decades, scientific inquiry have demonstrated skin to be a complex organ in which precisely regulated cellular and molecular interactions govern many crucial responses to our environment .Factors affecting the delicate homeostasis that exists among the skin cells results in conditions as diverse as wrinkles, hair loss, blisters, rashes and even life threatening cancers and disorders of immune regulation [(2)]

Definition-TUMOUR

Tumour or Neoplasm defined by Sir Rupert Willis [(3)] as an abnormal mass of tissue the growth of which exceeds and is uncoordinated with that of normal tissues and persists in the same manner even after the cessation of the stimuli that evoked the change or response.

CLASSIFICATION

Tumours on the whole may be divided into benign and malignant depending upon the histological features and certain biological behaviors.

Benign tumours show a high degree of structural differentiation usually composed of relatively well differentiated cells. The growth is slow, rarely shows limited degree of infiltration, does not usually metastasize and may

cease to grow spontaneously.

Malignant tumours show structural abnormalities such as abnormal size, shape, nucleus to cytoplasm ratio, rapid growth with atypical mitotic figures and they infiltrate the surrounding tissues at the expense of the normal structures and frequently metastasize.

The histological differences between the two may at times be rather difficult as the benign tumours may show the some irregularities as are found in malignant ones. On the other hand, metastasis may not occur in all malignancies.

More over new growths whose cells show definite malignant qualities may remain localized and may even heal spontaneously leaving the pathologist and clinician at loggerheads .For example keratoacanthoma one of the most rapidly growing skin tumours is benign but show malignant histopathological features. Next is basal cell epithelioma which is slow growing locally aggressive malignant tumour that ordinarily does not metastasize.

Genetic and environmental factors may play a role in the development of certain tumours.

Diagnosis of tumours has to be based on the history, clinical picture, histopathological examination with routine stains of haematoxyline and eosin and special stains and if needed histochemistry, fluorescent techniques and electron microscopic studies. In this study the history, clinical picture and histopathology have been the diagnostic procedures adopted.

Classification of SKIN TUMOURS

Tumors can arise from all the structures of epidermis, dermis or subcutaneous tissues and can be divided accordingly. In this study, the classification as in Histopathology of the Skin by LEVER 8 th edition is followed.

PRIMARY

1. Tumours of surface epidermis.
2. Tumours of epidermal appendages
3. Tumours of the fibrous tissues
4. Tumours of the vascular tissues
5. Tumours of the fatty, muscular and osseous tissue
6. Tumours of the neural tissue
7. Disorders of nevus cells and melonocytes.

SECONDARY

Metastatic carcinoma of the skin.

Skin tumours chosen for this study are

1. Tumours of the surface epidermis
2. Tumours of the appendages

Tumours of the surface epidermis which is classified as

A.BENIGN

1. Epidermal nevus

2. Seborrhoeic keratosis

    Irritated

    Adenoid

    Plane

    With an intraepidermal epithelioma pattern

    Melanoacanthoma

    Inverse follicular keratosis

    Benign squamous keratosis

3. Clear cell acanthoma

    (also nevus comedonicus, epidermolytic acanthoma, acantholytic acanthoma, oral white sponge nevus)

4. Fibro epithelial polyp

5. Warty dyskeratoma

6. Actinic keratosis

    (also precancerous leukoplakia, oral florid papillomatosis, Bowen's disease, erythroplasia of Queyrat)

7. Keratoacanthoma

    Giant keratoacanthoma

Keratoacanthoma centrifugum marginatum

Subungal keratoacanthoma

Multiple keratoacanthoma

Multiple eruptive keratoacanthoma

8. Benign lichenoid keratosis .

B. MALINGNANT

1. Squamous cell carcinoma

Spindle cell

Acantholytic

Verrucous

Horn forming

Lymphoepithelial

2. Basal cell carcinoma

Multifocal superficial (superficial multicentric)

Nodular (solid, adenoid cystic)

Infiltrating

Nonsclerosing

Sclerosing (desmoplastic morpheic)

Fibroepithelial

Basal cell carcinoma with adnexal differentiation

Follicular

Eccrine

Basosquamous carcinoma

Keratotic basal cell carcinoma

Pigmented basal cell carcinoma

Basal cell carcinoma in basal cell nevus syndrome

Micronodular basal cell carcinoma

C.CYSTS

Follicular cysts

Infundibular cyst

Trichilemmal cyst

Steatocystoma multiplex

Dermoid cyst

Eruptive vellus hair cyst

Milia

Bronchogenic and thyroglossal cyst

Cutaneous ciliated cyst

Median raphe cyst of the penis.

Tumours of the epidermal appendages are classified as

Lesions	Follicular differentiation	Sebaceous differentiation	Apocrine differentiation	Eccrine differentiation
Hyperplasia,	Hair follicle Nevus	Nevus Sebaceous	Apocrine nevus	Eccrine nevus
		Sebaceous hyperplasia		
Hamartomas, Cysts	Dilated pore			
Benign neoplasms	Trichofolliculoma	Sebaceous adenoma	Apocrine Hidrocystoma	Eccrine Hidrocystoma
	Pilar sheath acanthoma	Sebaceoma	Hidradenoma papilleriferum	Syringoma
	Fibrofolliculoma		Apocrine syringocystadenoma	Eccrine cylindroma
	Trichodiscoma			Eccrine poroma
	Trichoepithelioma		Tubular apocrine adenoma	Mucinous syringometaplasia
	Trichoadenoma			
	Pilomatricoma		Eruptive adenomatosis of nipple	Eccrine spiradenoma
	Proliferating trichemmal cyst			Nodular hidradenoma
	Trichilemmoma		Apocrine cylindroma	
	Tumour of the follicular infundibulum			Chondroid syringoma

Tumours of epidermis and cyst included in this study are

1. Seborrheic keratosis
2. Epidermal nevus
3. Epidermal cyst

4. Steatocystoma multiplex

5. Keratoacanthoma

6. Basal cell carcinoma

7. Squamous cell carcinoma.

The appendagel tumours included in this study are

1. Syringoma

2. Nevus sebaceous of Jadosshon

3. Trichoepithelioma

4. Sebaceous carcinoma

SEBORRHOEIC KEROTOSIS

(Syn. Senile wart, Seborrhoeic wart, Basal cell papilloma, Seborrhoeic verruca, Brown wart)

Study of Yeatman et al [10 a] on the prevalence of seborrhoeic keratosis in an Australian population reported the frequency of seborrhoeic keratosis in 100 adults in the age group of 15-25, 26-50 and above 75 years. There was an increase in prevalence of seborrhoeic keratosis from 12 % of 15-25 years old to 100 % in the age above 50 years. These are benign tumours composed of epidermal keratinocytes, and is frequently pigmented. It occurs more commonly in the elderly. It may also be seen in the younger age group. Multiple seborrhoeic keratosis may be a familial trait, autosomal dominant

mode of inheritance [5] .Its occasional association in the same patient with fibroepithelioma type of basal cell carcinoma suggest that it could be a nevoid tumour [6] as studied by Pinkus .H.et al.

A genetically determined predisposition based on mosaic pattern of aberrant response to epidermal growth factors and inhibitors would explain those cases where a profuse eruption follows an inflammatory dermatosis. It occurs as a manifestation of internal malignancy, usually cancer of gastro intestinal tract. The latter sign is named after Leser-Trelat. Tumour derived circulating growth factors or humoral factors may be involved in the pathogenesis of these lesions [9]. Higher prevalence of seborrhoeic keratosis on the sun exposed areas show that sunlight could be a factor in the etiology of the seborrhoeic keratosis [10].Because of the verrucous appearance of the lesions HPV has also been suggested as a possible etiology. Both sexes are equally affected.

Lesions can occur on any part of the body. But they are more common over the face, neck, upper trunk and they can be bilateral, symmetrical or asymmetrical. Classically it present as a verrucous plaque with stuck on appearance. The color is yellowish to light brown. Fully developed lesions are deeply pigmented and covered by greasy scales and are few millimeters to several centimeters in diameter.

Lesions over eyelids and flexures are occasionally pedunculated. Usually seborrhoeic keratosis asymptomatic, rarely itchy. Irritation or infection may cause swelling, bleeding, oozing, crusting, deepening of the color due to the inflammation .They do not involute spontaneously. Transient eruptive type

may be associated with erythrodermic type pitryasis rubra pilaris.

Clinical variants are stucco keratosis [12], as described by Willoughby C, Soter NA. a non-pigmented variant of seborrhoeic keratosis, occurring principally on the limbs and [13], dermatosis papulosa nigra occur commonly in the dark skin individuals, appear early in life and may be multiple in numbers over the face.

The lesions are mostly benign and malignant transformation to basal cell carcinoma, squamous cell carcinoma and bowens disease or anaplastic epithelioma occur rarely [14]. as studied by Cascayo CD Eval.

Multiple eruptive seborrhoeic keratosis known as Leser -Trelat sign is associated with multiple internal malignancies [15] like adenocarcinoma of the colon and breast. Others associated malignant tumours associated with seborrhoeic keratosis are lymphoma, leukemia and melanoma. Chemotherapy, particularly cytarabine can cause inflammation of the seborrhoeic keratosis, [16]. Heaphy JR et al malignant acanthosis nigricans present is 35% of patients with Leser- Trelat sign suggesting a similar mechanism of action [17].

Histological types

The histological sub types of seborrhoeic keratosis are

1. Acanthotic type- The most common
2. Melanoacanthoma type
3. Hyperkeratotic type

4. Adenoid type

5. Superficial type

6. Irritated type

7. Clonal type (representing an intra-epidermal epithelioma of Borst Jadosshon [18].

Histopathology

The common features are hyperkeratosis, acanthosis, and papillomatosis. The acanthosis is due to the upward proliferation of the epidermal cells and this is responsible for the stuck on appearance clinically. In the irritated type, squamous eddies are seen numerously. In adenoid type, numerous thin tracts of epidermal cells lined by double row of basaloid cells, extending from epidermis showing branching and interweaving in the dermis. In the acanthotic type, numerous true horn cysts and pseudo- horn cysts are seen. In hyperkeratotic type, numerous digitate upward extensions of lined papilla resembling church spires are seen .In the clonal type, numerous well defined nests of epidermal cells with small, dark stained nuclei are seen. In the melanoacanthotic type, numerous melonocytes are seen scattered throughout the tumour lobules intermingled with basaloid cells.

Treatment

1. Removal with a curette and the base may be cauterized or electro-coagulated or treated with haemostatic solution such as silver nitrate or ferric sub sulfate (Monsels Solution).

2. Application of cryotherapy.

3. Painting the lesion with the Trichloro- acetic acid

4. Surgical excision is not usually indicated except when malignant melanoma is considered as differential diagnosis and when the lesion is large and not responding to other modes of treatment.

5. Laser therapy.

6. Topical 5-Flurouracil and dermabrasion. [19].

VERRUCOUS EPIDERMAL NEVUS

(Syn. Nevus verrucous, linear verrucous nevus, linear epidermal nevus.) The term nevus denotes a circumscribed congenital developmental abnormality resulting in faulty production of mature and nearly mature structures.

Epidermal nevi are hamartomatous lesions arising from embryonic ectoderm.

The pluripotent ectodermal cells evolve into a variety of differentiated cell types, including keratinocytes and cells forming the various appendages .Most of the cases occur within the first years of life, rarely reports of elderly, with the oldest being 60 years of life [21] as described by Adams DF et al.

Verrucous epidermal nevus is a circumscribed hamartomatous composed almost of keratinocytes. These arise due to the genetic mosaicism. [21].Mosaicism appears due to the post-zygotic chromosomal non-disjunction during mitosis or from somatic mutation occurring early in the embryonic life. Also, verrucous epidermal nevi having the histological features of epidermolytic hyperkeratosis reflects the gene mutation.

Verrucous epidermal nevi occurs at any site but uncommon in face and head, where nevus sebaceous are more common .Lesions may be single or multiple .They follow the lines of Blaschko [22]. On the trunk, they are transverse bands, lesions virtually never cross the midline, but the lesions close to the midline take the course of vertical direction. Lesions in the limbs are more linear unilateral distribution is more common than bilateral and the lesions may form irregular warty or geometric patterns. Mucous membranes may be affected.

Linear nevi are seen clinically as hyper pigmented warty growths arranged in linear plaques. Linear nevi may be localized or systematized .The localized type presents at birth with only one linear lesion. It consists of closely set hyperkeratotic papules anywhere in the body. Nevi along the long axis in unilateral fashion is called as nevus unilateris. In this form it resembles ILVEN (Inflammatory linear verrucous Epidermal nevus) .But the latter differs from it clinically by the presence of erythema and pruritis and histologicaly by the presence of parakeratosis and inflammation.

The color of the nevus unilateris is greyish yellow, associated with warty fissured surface .In most cases, the lesions are longitudinal or spiral over

the extremities and some acquire a circular or stellate shape over the face. It may be associated with woolly hair [23] and megalopinna [24].In addition this nevi may also be seen in Proteus syndrome, Child syndrome [25], Mac- Albright syndrome [26] and in Klippel-Trenaunay syndrome [27].It may be associated with multiple myofibromatosis in a child with NF-1 sometimes widespread, linear lesions in a parallel arrangement bilateral symmetrical extensive geometric patterns occur especially over the trunk is called as ichthyosis hystrix [28] . Occasionally, basal cell epithelioma is observed particularly on the head, in the case of linear epidermal nevi associated with either a nevus sebaceous or a syringocystadenoma papilliferum [29].Similarly squamous cell carcinoma, bowens, reported rarely [30] .But in one instance it metastasized to the region lymph node [31].

A study conducted by Vidaurria La et al [25a] reported 35 cases of epidermal nevus syndrome seen in National Institute of Pediatrics' in Mexico during a 31 year period. It represented 7.9 % of 443 patients with epidermal nevi. Of importance is the association of nevi with other defects, i.e. skeletal deformities and central nervous system abnormalities such as mental retardation, epilepsy, neural deafness and increase incidence of various types of hemangiomas, collectively called as Epidermal nevus syndrome [32] as studied by Solomon et al.

Histopathology

It can be divided into two types

1. Epidermolytic hyperkeratosis
2. Non -epidermolytic hyperkeratosis.

The common features are hyperkeratosis, acanthosis, papillomatosis, and elongation of rete ridges.

Epidermolytic type or granular degeneration of epidermis shows

1. Compact hyperkeratosis
2. Perinuclear vacuolization of cells in the granular and spinous layer.
3. Peripheral to the vacuolization is indistinct cell margins
4. An increased number of irregular shaped, large keratohyaline granules.

Some lesions show distinct church spire pattern of acanthosis and hyperkeratosis resembling acrokeratosis verruciformis and Seborrhoeic keratosis. Very rarely it also shows focal acantholytic dyskerotosis. Rarely it may shows the features of viral warts, acanthosis nigricans, verrucous phase of incontentia pigmenti [(34)] as described by Fletches Vs Williams, Lone et al.

Treatment

It is wise to delay the therapy as the final extent of the process cannot be determined, failure to do so may result in the appearance of new lesions in adjacent site to the treated area.

Small linear lesions can be excised. Improvement is achieved by the use of electro-desiccation or Cautery.Hypertrophy scarring or keloidal formation can complicate this modality of treatment. Cryotherapy or CO2 laser has given inconsistent results. The only effective treatment of this nevi is surgical excision.

Solid CO2 laser, tri chloro acetic acid , radiation, have been tried. Topical treatment include podophyllin, retinoic acid, anthralin, calcipitriol are used, but relatively ineffective. Occasionally, using combination therapy will lead to higher efficacy.

Systemic retinoids can produce a partial but usually temporary response in some patient with extensive disease.

EPIDERMAL CYST

(SYN: Epidermoid cyst, epithelial cyst, keratin cyst, sebaceous cyst, infundibular cyst, epidermal inclusion cyst)

It is the most common of all the cysts .They result from the proliferation of the surface epidermal cells lying within the dermis. Production of keratin and lack of communication with the surface are responsible for the cyst formation. Most epidermal cysts arise from the occluded pilosebaceous

follicles as described by Mc.Gaven and Binnington in 1966.Some of them arise from traumatic displacement of epidermal cells into the dermis. Those occurs as a part of Gardener syndrome and of nevoid Basal cell carcinoma are probably due to the developmental defects. They arise spontaneously. Ohinis [56] confirmed the cytokeratins profile of HPV 57, 60, in palmo-plantar epidermal cyst [57] as described by Egawa keraj et al.

Epidermal cyst may occur during puberty or in adult life and affect both sexes. Epidermal cyst are frequently seen over the face, scalp neck, shoulder, and trunk. It may be solitary or multiple. In Gardeners syndrome numerous epidermal cysts occur especially over the scalp and face. Traumatic inclusion cysts usually occur over the palms, soles, buttocks or knees. Epidermal cysts are slow growing cysts, elevated, round, firm, intradermal or subcutaneous tumours. They are dome shaped protuberances that are mobile over the deeper structures. They are tethered to the overlying epidermis and occasionally they may show central keratin filled blackish or bluish punctum. A clinico pathological study conducted by Chandrasekaran et al [56a] reported the 34 epidermal cysts. Among them 40 % had punctum. Upon rupture a cheesy, odoriferous material may be expressed. Rarely malignant transformation may occur [58] as described by Delaretz J.

These may go for complications like secondary infection, predominantly by anaerobes [60] and dystrophic calcification.

Histopathology

The cyst wall is composed of all the layers of epidermis in the dermis and the lumen is filled with laminated keratin. In sectioning with haematoxyline and eosin melonocytes and melanin pigment of keratinocytes in the contents of cyst can be seen. Rupture of the cyst into the dermis elicits a foreign body granulomatous reaction-keratin granulomas containing numerous multinucleated giant cells.

Malignant degeneration of the epidermal cyst is interpretated either as pseudo carcinomatous hyperplasia in a ruptured epidermoid cyst [(63)] or as a proliferating trichilemmal tumour [(64)].

Treatment

Complete surgical excision is required if the cyst becomes symptomatic. However, if a portion of wall is left the cyst can recur. An inflamed cyst is better incised & drained and phenolised. Destruction of the cyst wall by a sharp curette, chemical cautery or electrodessication produces less consistent results. An inflamed, non-infected cyst can be treated by intralesional triamnicinolene 5mg per ml[(63)] .

STEATOCYSTOMA MULTIPLEX

(Syn: Sebocystomatosis, Epidermal polycystic disease) Steatocystoma multiplex was first described by Pringle in 1899[(65)] .Several cases have been inherited as autosomal dominant trait [(66)] .Occasionally if it occurs as a solitary, non inherited, in adults it is called as simplex type[(68)] . A

clinico pathological study of 64 cases of steatocystoma multiplex by Cha .S. et al at [128] department of dermatology ,Seoul, Korea reported most of the cases were sporadic, average age being 26 years and the distribution over the chest arms and axilla. It occurs due to the mutation in keratin 17 gene.

It is a rare disease with multiple cysts of skin .Men are affected more in the previous studies but now both sexes are equally affected .The lesions may present from birth or develop at puberty or shortly after that . The lesions are usually located over the upper trunk, especially over the sternum, axilla, arms ,face and sometimes over the scrotum. The lesions are numerous, small, round, soft to firm cystic nodules adherent to the overlying skin and measure 1-3 mms in diameter. The color varies from the flesh color to yellowish .If punctured the cysts discharge an oily fluid in some instances. The lesions are asymptomatic but secondary inflammatory changes may occur with suppuration and scarring. No punctum is apparent over the cyst, but there may be widespread comedones. Associated conditions are acrokeratosis veruciformis, hidradenitis, hypohidrosis, hypothyrodism, hypotrichosis, lchthyosis, koilonychias, pachyonchia congenita[(73)] and lichen planus. It is also associated with natal teeth.

Histopathlogy

The cyst wall is intricately folded consisting of several layers of epithelial cells and the central portion consists of homogenous horny layer that protrudes irregularly in to the lumen.

Characteristic feature is the presence of flattened sebaceous glands lobules either within or close to the cyst wall. Occasionally cysts contain lanugo hair [91].

Histogenesis

It has been suggested that differentiation in the cyst wall of steatocystoma is to a large extent in the direction of the sebaceous duct and sebaceous gland[92] .

Treatment

It is usually asymptomatic. Cosmetic surgery may be helpful in selected instances. For extensive cases, dermabrasion may be useful.Isotretinoin can be useful in suppurated cases [77] .The best treatment for these lesions in face is inserting a needle and extripating the contents without removing the cyst wall.

KERATOACANTHOMA

Syn: Molluscum sebaceum, Molluscum pseudocarcinomatum, Tumour like keratosis, Self healing primary squamous cell carcinoma, Button epithelioma , Idiopathic cutaneous pseudoepitheliomatous hyperplasia [35].

A rapidly evolving tumour of the skin, composed of keratinizing squamous cells originating in pilosebaceous follicles and resolving spontaneously if untreated. It was first described by Sir Jonathan Hutchinson in 1889,who called this tumour as crateriform ulcer of the face [37]. The term Keratoacanthoma was first officially adopted in 1950 by Rook and Whimster[36] .

Males are affected three times more then the females .Mostly it occur in adult life, peak age between 55-65 years. But familial type occurs after or during puberty and a neonatal case has been reported [38] .Study conducted by Sean et al reported that 2 cases of keratoacanthoma developed at the sites of previous trauma.[42 a]

The relationship between keratoacanthoma and squamous cell carcinoma is not clear yet. Some authors still maintain that this represents a benign epithelial tumour distinct from squamous cell carcinoma whereas others hold that it is a variant of squamous cell carcinoma with tendency to spontaneous regression but with the potential for distant metastasis and may be fatal to the patients. Recent publications on loss of heterozygosity and on expression of angiotensin type 1receptor and of desmoglein 1and 2 showed differences between this and squamous cell carcinoma revealing different phenotypes of these two tumours[41] .

Keratoacanthoma arises due to multiple factors. Chronic UV light exposure [42]can increase the risk of keratoacanthoma .The relation between this and chemical carcinogen has been well documented in humans and several animals.

Smokers seem to be more affected than non-smokers, trauma in the form of arterial puncture, vaccination, could be a factor .Recently evidence of HPV was documented by PCR and the associated types are 25, 48, 19.Keratoacanthoma is also common in HIV patients [44] .Mutation in the p53 gene results in the development of this tumour [46] Cyclins regulating the cell cycle and mitotic activity may also play a role [47]. in the development of this

tumour. Anti-apoptotic bcl-2, growth regulatory cytokines oncostatin M and the cyclin dependent Kinase inhibitor p27 have been suggested to play a role [48] .These lesions are common in the sun-exposed areas. The characteristic feature is the lesion grows rapidly within a few weeks and subsequently showing a slow involution over a period of a few months.

Clinically keratoacanthoma are divided into three stages have been described- proliferate, mature and resolving. Ghadially [43] divided mature Keratoacanthoma into Type1- Bud shaped Type2- Dome shaped Type3- Berry shaped Regressing lesions are characterized by a keratotic, partly necrotic nodule that becomes progressively flat upon elimination of the keratotic plug eventually leaving an hyper pigmented scar. It can be associated with Muir-Torre syndrome and colorectal cancer syndrome, xeroderma pigmentosum, lympamatoid papulosis.

Variants of Keratoacanthoma are giant type, centrifugum marginatum type, multiple (Ferguson-Smith), generalized eruptive type-Grzybowski, subungal type and mucosal type.

Histopathology

The overlapping features between this tumour and squamous cell carcinoma render differentiation very difficult or even impossible in some cases. In early lesions epidermis is markedly hyperplastic and central keratotic plug is not as pronounced as in fully developed lesions. There may be fewer atypical cells at the lower margin.

Mature lesions show a large central core of keratin surrounded by a well differentiated proliferation of squamous epithelium resembling squamous cell carcinoma. The epidermis at sides of the central core extends as the keratotic area in a fashion that has been described as buttressing. Inflammatory infiltrate consists of lymphocytes, histiocytes, plasma cells and eosiniophills seen .In resolving lesions thick of the epithelial proliferation decease and the tumour becomes more flattened and less keratotic.

Treatment

It shows a tendency to spontaneous regression. Surgical excision is the treatment of choice. Mohs micrographic surgery have been adopted for difficult cases like recurrent lesions, giant lesions or lesions of centrifugum marginatum which cover a large area of the body. Curettage followed by electrodessication or cryosurgery has been used with low rate of recurrences. Radiotherapy is also useful, like electron beam therapy, orthovoltage radiation and supercial X-rays. Intralesional methotrexate, bleomycin, 5-Flurouracil, also useful in some patients [(53).] Latest mode of treatment is Photodynamic activation with AMINOLEVULENIC ACID [(54)] .

BASAL CELL EPITHELIOMA

(Syn: Rodent ulcer, Jacobs's ulcer, Basiloma)

Basal cell epithelioma was first described by Jacob in 1827.Krompecher in 1903 found out that the tumour arises from the basal cells of the epidermis. Geschickter and Koehler called basal cell carcinoma as -appendageal cell carcinoma.

Mallory suggested that they are carcinomas of hair matrix cells. Foot in 1947, reported that they are carcinomas arising from distorted primordial adnexal-hair, sebaceous or sweat gland [98] .Adamson in 1914, stated that these are nevoid tumours originating from latent embryonic foci aroused from their dormant state at a later period of life, either from embryonic pilosebaceous follicles or from embryonic sweat ducts. Wallace and Halpert in 1950 described that they were benign tumours of the hair matrix,differentiated to the hair follicle and called them trichoma.[99]. According to Lever they were nevoid tumours or hamartomas arising from the primary germ cells. Pinkus suggested that basal cell carcinoma occurring in latter life arises from pluripotent cells that form continuously differentiating into hair sebaceous sweat gland.

Histologicaly there are two arguments against metastasis of basal cell carcinoma. (1).Lack of autonomy of tumours, which has been experimentally proved by auto transplants of basal cell carcinoma , where they fail to survive unless the connective tissue stroma was included .(2).Electron microscope shows monotony of cells which speaks against their nature and they resemble cells of undifferentiated hair matrix [100] or primary epithelial germ cells of embryonic epidermis[101] .

Predisposing factors

1. Prolonged exposure to the sunlight (light skin color) [103].
2. Large doses of Radiation to the face and even to the spine.
3. Prolonged intake of inorganic arsenic

4. Thermal injury to the skin and the scars of tuberculosis cutis and small pox vaccination [104]

5. Genetic factors: the nevoid basal cell epithelioma syndrome-autosomal dominant inherited condition.

6. Experimentally, basal cell carcinoma it was produced in rat by the application of anthralin to the unshaven skin of the back. Tumours was seen 4-5 months after the application [105] .

Mainly they occur over the hair bearing skin. Face is the commonest region where it can involve the inner canthus of the eye, bridge of the nose, along the imaginary line from the tragus of the ear lobe to the angle of the mouth. Oral mucosa may be involved in occasions. They may however occur on some uncommon sites such as scars of small pox, chickenpox vaccination and of discoid lupus erythematosus, sites of chronic leg ulcers, burns scars, the palms and soles from the pilonidal sinus and the vulva. The lesions are usually solitary but multiple lesions are the rule in the nevoid basal cell carcinoma syndrome, linear unilateral basal cell nevus and in the xeroderma pigmentosum. It is common in adults and rare in children. There is no sex predilection but males are slightly more affected due to the factors of occupation and sun exposure and Basal cell carcinoma is more common in light colored races.

CLINICAL CLASSIFICATION

Clinical types of basal cell carcinoma are

1. Nodulo-ulcerative

2. Pigmented

3. Fibrosing / Sclerosing / Morphoea like

4. Superficial

5. Fibroepithelioma

Clinical syndromes

1. Gorlins syndrome

2. Linear unilateral basal cell nevus

3. Bazex syndrome.

Christenson et al [100a] conducted a study at department of dermatology, Mayo clinic, Rochester. They included the persons less than 40 years of age in Olmsted county, Minnesota, to evaluate the sex and age specific incidence of basal cell carcinoma and squamous cell carcinoma. During this study 451 incident basal cell carcinoma were diagnosed in 417 patients and 70 incident squamous cell carcinoma in 68 patients. Of these 328 were histologicaly confirmed basal cell carcinoma and 51 were histologicaly confirmed squamous cell carcinoma. Nodular basal cell carcinoma was the common subtype. The age adjusted incidence of basal cell carcinoma was more for women than in

man but in squamous cell carcinoma the incidence was similar in both sexes. Nodulo-ulcerative type-begins as a small waxy nodule that often shows a few small telengiectatic vessels on its surface. The nodule slowly increases in size and undergoes central ulceration and is surrounded by pearly, rolled out borders-classical rodent ulcer. Occasionally they invade deeply, destroying eyes, nose, cartilage and even the dura matter by penetrating the skull[110] .

Pigmented type-differs from the above only by the brown pigmentation of the lesion due to the proliferation of melanocytes in the tumour. Fibrosing type-manifests as solitary, flat or slightly depressed indurated yellowish plaque with smooth and shiny surface and ill-defined border, almost on the face. Superficial type -consists of one or several erythematous scaly, slightly infiltrated patches that slowly increase in size and are surrounded by a fine thread like pearly borders. They show small areas of superficial ulceration and crusting and the center may show, atrophic scarring. This type commonly occurs on the trunk.Fibroepithelioma of Pinkus-consist of one or several raised firm pedunculated nodules covered by erythematous skin and commonly located on the back.

GORLINS SYNDROME

(Nevoid Basal Cell Epithelioma Syndrome)

Gorlin in 1963 reported multiple basal cell carcinomas associated with milia, epidermal cysts, abnormal ribs, dental cysts, characteristic facies and scoliosis, kyphosis, short metacarpals, supernumerary digits, keratosis of palms and soles, agenesis of corpus callosum, dural and periventricular calcification,

ovarian fibromata, cataract, hypogonadism, mental deficiency, congenital hydrocephalus and occasional cerebellar medulloblastomas and calcium deposits in the skin. Rarely fibro sarcoma of the mandible[111] and ameloblastoma of the lower jaw may occur.

Numerous supercial pit like depressions of palms and soles 1-3mms in diameter, constitute one of the hallmarks of this syndrome. They occur in 2nd decade of life or later and they represent forme frusta of basal cell carcinoma.

LINEAR UNILATERAL BASAL CELL NEVUS

This nevus is a rare condition non inherited, consists of unilateral linear or zosteriform eruption of basal cell carcinoma, comedones, cysts and striae like areas of atrophy [113]

BAZEX SYNDROME

Described first in 1966, is an autosomal dominant inherited condition shows follicular atrophoderma, characterized by widened follicular openings like ice pick marks mainly on the extremities and multiple small basal cell carcinoma on the face arising in the childhood, adolescence or early adulthood [114] .In addition localized anhidrosis, generalized hypohidrosis and congenital hypotrichosis on the scalp as well as elsewhere also is seen.

Histopathology

The characteristic cell is the basalioma cell with a large oval or elongated nucleus and relatively little cytoplasm. The cells do not show any inter-cellular bridges by the light microscope. The nuclei are uniform in size

and staining. The connective tissue stroma is arranged in parallel bundles around the tumour masses.

The stroma appears mucinous and reacts metachromaticaly. There are retraction clefts around the tumour masses and lacunae are due to the absence of the bullous pemphoid antigen[115] . A mild inflammatory infiltrate may be seen but dense lymphocytic infiltrate is usually seen if the lesion clinically shows ulceration.

From the histological point of view basal cell carcinoma divided into 3 groups

- Solid or undifferentiated
- Differentiated
- Mixed

Undifferentiated

- Circumscribed, infiltrative

Differentiated

- Keratotic
- Cystic
- Adenoid

Solid basal cell carcinoma shows, tumour masses of various sizes and shapes embedded in the dermis.The peripheral cell layer of the tumour mass shows a pallisading pattern where as the nuclei of the cells inside lie in the haphazard fashion.

Keratotic type:

This type show parakeratotic cells and horn cysts in addition to the undifferentiated tumour cells. The parakeratotic cells have an elongated nuclei and eosinophilic cytoplasm- lies in the strands, concentric whorls or around the horn cysts and the latter contain fully keratinized cells and represent attempts of hair shaft formation.

Cystic type:

This type shows cystic spaces within the tumour lobules. The cyst formation is due to necrobiotic changes of tumour cells. The cells in the centre show a vesicular appearance suggesting differentiation into sebaceous cells.

Adenoid type:

This type shows tubular or glandular like structures. The cells arranged in interwining strands resulting in a lace like pattern. The lumina are filled with a colloid substance or an amorphous granular material . The degree of differentiation is low that even with histochemistry, it is not possible to say whether the differentiation is towards apocrine or eccrine glands.

There are 4 uncommon **histological variants** of basal cell carcinoma

1. Adamantinoid type-resembles dental adamantinoma
2. Granular type-resembles granular cell tumour
3. Clear cell type-contains glycogen vacuoles in cytoplasm
4. Matricial type -shows shadow cells as in pilomatricoma.

Therapy

According to Pillsbury states the cure rate as 100% when the lesion is recognized and intervened rapidly. The choice of therapy depends on the site the size and the number of lesions. The success of therapy depends on early recognition, accurate histological typing and the method of treatment. The therapy is not satisfactory when the basal cell carcinoma involves the orbit, nose or ear.

METHODS OF TREATMENT

1. Surgery If the lesion is large-wide excision followed by either full thickness graft or Curettage and cauterization must be done by a competent plastic surgeon.
2. Mohs Micrographic Surgery This method is used following curettage &desiccation to determine the clear zone in cases of invasive and infiltrative tumour in difficult sites.
3. Cryosurgery with liquid nitrogen

4. Curettage and cauterization. This method is widely used for the elderly and small early lesions less than 1cm.Recurences are rare.

5. Dermabrasion. It is simple and safe procedure for small early lesions. No scarring is reported.

6. Radiotherapy.This is best for elderly and for extensive tumour lesions especially involving inaccessible sites (eyelids).Scarring is seen but recurrences are rare. Radiotherapy is contraindicated for recurrent lesions and Morphoeic type of basal cell carcinoma which is radio resistant.

7. Combination therapy : Surgery + Irradiation of the lesion.

8. Local cytotoxic therapy

    a. Topical 20% 5-FU ointment

    b. Topical 20% Podophyllin resin

    c. Intra lesional injection of aqueous solution of 0.5% - 5% 5-FU

9. Interferon therapy and photodynamic therapy are useful.

SQUAMOUS CELL CARCINOMA (SCC)

It is a malignant tumour arising from the kerartinocytes of the epidermis. Pott was first to describe the malignant nature of the squamous cell carcinoma in 1775 [(115)] .Squamous cell carcinoma is strongly associated with advanced age

with a sharp increase in Incidence after the age 40. It is twice common in men than women, probably as a result of greater lifetime Ultraviolet exposure in men. There is an inverse relationship between skin pigmentation and squamous cell carcinoma incidence, largely because of the protective effect of eumelanin. Melanocortin-1 receptor, is a major determinant of skin pigmentation and hair color. Several variant of MCIR alleles are associated with increase of squamous cell carcinoma that was independent of skin type and hair color. MCIR gene is highly polymorphic with more than 20 variants [(118)].

Nuzhat Yauman et al studied 75 cases of malignant skin tumours of which squamous cell carcinoma were 30 cases, basal cell carcinoma were 36 cases malignant melanoma 5 cases, bowens disease 1 case and malignant trichilemmoma 1case [125 a]

Predisposing factors

1. UV exposure
2. Ionizing radiation
3. Environmental carcinogens
4. Immuno suppression
5. Scars
6. Burns or chronic heat exposure

7. Inflammatory dermatosis

8. Precursor skin lesions (angiokeratoma, bowens disease)

9. Genodermatosis (Xeroderma Pigmentosa, Porokeratosis)

10. Human papilloma virus

Genetic alterations

Most analysis of genetic alterations in squamous cell carcinoma have been performed in cases of oral or head/neck Squamous cell carcinoma. Chromosomal deletions commonly involve chr-3, 9, 11, 17, The regions most commonly include 9p21 and 17p13 where the P161-nk4a and are respectively located [119].

In addition to p53 dysregulation of bcl-2, Bax apoptotic regulatory proteins have been described [121] .Also the inhibitor of apoptosis protein survin is expressed both in Squamous cell carcinoma and precursor lesion [122]. In one study its expression correlated with aggressive tumour phenotype.

In white men and women, the majority of Squamous cell carcinoma occur on sun exposed areas. Squamous cell carcinoma of the legs is more common in the women, in blacks, Squamous cell carcinoma occurs equally in both sexes on sun protected areas in immunosuppressive patients, who may manifest eruptive squamous cell carcinoma.

Squamous cell carcinoma presents as a firm, flesh colored or

erythematous keratotic papules or plaque, but squamous cell carcinoma also sometimes will be pigmented. Other presentations of squamous cell carcinoma are ulcer, nodule and as cutaneous horn .the tumour also presents as verrucous or abscess like lesions particularly if in periungual region. Margins may be distinct, firm, elevated. Progressive tumour invasion ultimately results in fixation to the underlying structures.

Lymph node involvement may be present and is due to the metastasis. Oral squamous cell carcinoma presents in patients with long history of smoking, tobacco chewing and alcohol abuse. Squamous cell carcinomas of the oral cavity are common in males, palate, and tongue are the most common sites. Oral squamous cell carcinoma most commonly evolve from lesions of erythroplakia and it is usually asymptomatic and presents as persistent, rough, patch or plaque that ultimately becomes firm and nodular. Lower lip Squamous cell carcinoma begins as a papule of actinic chelitis or scaly leukoplakia with slow progression to a tumour nodule.

Squamous cell carcinoma of the vulva most commonly occurs on the anterior labia majora, beginning as a small warty nodule or as an erythematous plaque.

Squamous cell carcinoma can arise from LSA of the vulva.HPV-16 may play a role in the etiology of Squamous cell carcinoma of uterine cervix.

Scar Squamous cell carcinoma begins in the scars typically after decades.

They are common in the lower extremities at the sites of chronic

pyogenic or venous stasis ulcers.

Verrucous carcinoma is a slow growing exophytic tumour with cauliflower like appearance that develop at the sites of chronic irritation[125]. Four types are present in the verrucous carcinoma;

1. Oral florid papillomatosis
2. Anogenital type
3. Epithelioma cuniculatum
4. Sites including scalp, trunk, extremities.

Detection of HPV-6, 11, 16, 18, in Epithelioma cuniculatum and HPV-2 in oral type of verrucous carcinoma raises the possibility that these tumours evolve from verruca vulgaris.

Metastatic Squamous cell carcinoma-signaled by palpable lymph node near the sites of squamous cell carcinoma or it may present as a large keratotic papules or nodules similar to the primary lesion.

Histopathology.

The hallmarks of invasive squamous cell carcinoma are the extension of atypical keratinocytes beyond the basement membrane and into the dermis, the absence of connection between tumour cells and the epidermis . In every case it is better to note the clues that may indicate a precursor lesion.

Tumours appear as single mass or small group of nests of cells. The lower border may broadly impose on the dermis or be represented by individual foci of micro invasions. Invasive tumour is confined to dermis, subcutaneous involvement is unusual. There are typically varying proportions of normal appearing and atypical squamous cells with increased mitosis, aberrant mitotic figures, nuclear hyperchromasia and loss of intercellular bridges. Squamous differentiation is seen as a foci of keratinisation, concentric rings of squamous cells called horn pearls. Loss of differentiation is associated with decreased keratin production.

Histological grade of Squamous cell carcinoma is **BRODERS** classification based on the presence of undifferentiated cells.

Type 1. <25%

Type 2. <50%

Type 3. <75%

Type 4. >75%

Histological subtypes

1. Adenoid type-tubular microscopic pattern and keratotic acantholyis

2. Clear cell type-keratinocytes appears clear as a result of hydrophic cytoplasmic swellings and accumulation of lipid vacuoles

3. Spindle cell type-spindle shaped atypical cells

4. Signet ring type-rare with concentric rings composed of keratinocytes and large vacuoles corresponding to dilated endoplasmic reticulum

5. Basaloid type

6. Verrucous type-Acanthosis and papillomatosis are more

7. Mucinous type.

Diagnosis is by skin BIOPSY. In most cases squamous ell carcinoma could be diagnosed by staining for cytokeratins. Metastatic rate of Squamous cell carcinoma is 0.5-6% [126]. It is common in tumours that are large, recurrent and if it is involving the deeper structures.

High risk Squamous cell carcinoma

1. Diameter >2cms

2. Depth >4mm

3. Tumour involving the bone, muscle and bone

4. Location –ears, lips

5. Tumour arising from the scars

6. Broder type 3, 4.

7. Immuno suppression

8. Absence of inflammation.

Therapy

1. Surgical excision-wide excision with a clear margin of 4mm, if the lesion <2mm and 6mm if the lesion >1cm

2. Mohs microsurgery surgery-for high risk cases

3. Radiation- for superficial, small lesions.

Rave et al [127] studied the response to the treatments and its recurrent rate. From Mohs-3.1% Excision -8.1% Radiation-10%

Follow-up

It should be regular, once in every 3 and 12 months and lymph nodes should be monitored for metastatic disease.

SYRINGOMA

(Syn: Syringocystoma, Hidradenoma eruptives)

Patrizi et al reviewed 29 cases of syringoma of which only one patient complaints of itching, two cases had solitary lesions, six patients had only eye involvement and eighteen patients were eruptive syringoma [94a]. Syringoma are benign adenomas arising from the intra-epidermal portion of the eccrine sweat duct.

Syringoma occurs predominantly in women at adolescent age or later in life .The lesions are multiple but solitary type is also reported .They are small skin colored, soft elevated, flat topped papules of size 1-5mm in diameter with angular outline.

They are commonly seen in bilateral symmetrical pattern below the lower eyelids but may also occur in cheeks, neck, axilla, trunk, abdomen and rarely vulva [91]

Classification

1. Multiple 2. Solitary 3. Eruptive

4. Unilateral 5. Occult 6. In apparent

7. Annular 8. Acral 9. Chondroid

Plaque type has also been reported so far only 7 cases are reported. [94].In eruptive type the lesions arise in great numbers, in successive crops on the anterior trunk and upper extremities in young persons It has also been reported in patients with Downs syndrome [93]. Unilateral type may occur rarely in the face or upper chest.

Occult type occurs in scalp in association with diffuse thinning of hair or cicatricial alopecia. Inapparent type have also been described as incidental finding in close approximation with basal cell carcinoma. Annular type is the one in which the papulesare arranged in the annular fashion in the trunk .Acral type are of multiple lesions appear as symmetrical grouped erythematous papules over the dorsa of fingers and hands in young men.

Histopathology

It shows numerous small cystic ductular structures lined by two rows of flattened epithelial cells, where the inner row of cells are vacuolated.. These cystic ducts are embedded in dermal fibrous tissue stroma. The lumina contains amorphous debris. Some of the ducts have tail like projections of epithelial strands into the fibrous stroma giving a typical Tadpole or Comma like appearance .In addition solid strands of basophilic epithelial cells are also seen independent of ducts. There is also a distinctive clear cell variant with an epithelial lining consisting of cells with largecytoplasm and glycogen. This type is associated with diabetes mellitus [95].

Histogenesis

Enzymes, histochemical and EM studies have established syringoma as a tumour with differentiation directed towards intra epidermal eccrine duct. Histochemical examination of syringoma tumour cells shows strongly positive reaction for eccrine enzymes namely succine dehydrogenase, phosporylase, and leucine aminopeptidase.

Therapy

Required mainly for cosmetic reasons.ElectroCautery, chemocautery, and dermabrasion are found to be useful. Cryo cautery is usually not indicated because the lesions are near the eyes. But in other sites it can be used. Surgical excision can be done for solitary large lesion [96] .

Chondroid syringoma

A special type-a benign tumour of eccrine sweat gland with stromal participant. Clinically, the tumours are firm, intradermal or subcutaneous nodules occurring most commonly on the head and neck and of size 0.5 to 3 cms in diameter [97].Rarely malignant transformation may occur. Microscopically there are 2 types –with tubules and cysts and the other-with small tubular lumen lined by single row of flat epithelial cell with small comma like projection into the stroma resembling Syringoma. The stroma contains plenty of mucin deposition.. Electron microscope shows an eccrine orgin that the chondroitin sulphate is produced by myoepithelial cells of eccrine structure.

Therapy

Complete excision of the lesion will be the best method of choice.

NEVUS SEBACEOUS

(Syn: Organoid nevus, Nevus Sebaceous of Jadosshon)

Jadosshon's definition of the organoid nevi is stable localized malformation of the skin through excess or deficiency of one or more of the normal mature constituents such as hair, glands , epidermis, or connective tissue and it excludes adenomas and often, less mature tumours. The evolution of nevus sebaceous includes 3 stages, 1. Early stage in infancy and childhood often characterized by under development of the hair and sebaceous glands.

2. An intermediate stage, usually begins with puberty and leads to the development of the glands and maturation with papillomatous hyperplasia. 3.

Late stage is due to the complications; development of the benign and malignant tumours.

Chang,Yi et al [80a] done a clinico pathological study of nevus sebaceous of 104 cases. Among them 48 were males and 56 were females. The age ranged from 3-60 years, but the mean age was 23.5 years. Most of the nevus sebaceous developed before 10 years (83 %).Most common site was scalp (70 %). This nevus is seen at birth or may appear in early life as a solitary lesion usually located on the scalp or face. In the childhood, it consists of circumscribed slightly raised, hairless plaque, often linear in configuration. At puberty, the lesion becomes verrucous and nodular. Some patients may show associated features of epilepsy, mental retardation, neurological defects, skeletal defects called as nevus comedonicus syndrome. Nevus may appear sporadically. Familial nevus has been described but is exceedingly rare [(80)] .

Histopathology

In the first few months of life, the sebaceous glands are well developed.Thereafter in childhood they regressed and reduce in size and number. The presence of incompletely differentiated hair structures is typical of this nevus. Some hair follicles consists of dilated, keratin filled infundibula showing multiple buds of undifferentiated cells. At puberty .large number of mature sebaceous glands with papillomatosis and hyperplasia of the epidermis are seen which is the characteristic feature.

Mature apocrine glands are also present. In adults various types of appendage tumours develop secondarily within the lesions of nevus commonly

syringocystadenoma papilliferum and less commonly nodular hidradenoma, syringoma, chondroid syringoma, sebaceous epithelioma, trichilemoma and proliferating trichemmal cyst. Rarely, basal cell carcinoma, squamous cell carcinoma, apocrine carcinoma and malignant eccrine poroma have also been reported .Mutations in the PATCH gene is reported for basal cell carcinoma in the sebaceous nevus [82]

Histogenesis

The frequent association of nevus sebaceous with appendageal tumours and apocrine glands suggest that nevus is derived from primary epithelial germ cells.

Therapy

Surgical excision with primary closure can be done. Lesions can be removed by tissue expansion technique. Dermabrasion and CO2 laser are also effective but recurrence is possible [83].

TRICHOEPITHELIOMA

(Syn: Brooke's tumour, Milia with telengiectasia, Epithelioma adenoids Cysticum, Benign cystic epithelioma)

A benign neoplasm with differentiation directed towards hair structures, particularly follicular germs. Trichoepithelioma is classified as –solitary and multiple.

Solitary

- Classical
- Giant
- Desmoplastic.

Multiple trichoepithelioma is due to the mutation in the gene CYLD [(87)]. Ziprkowski et al conducted a study in trichoepithelioma in which 50 % of the patients had family history of trichoepithelioma.[85a] Multiple trichoepithelioma is transmitted as autosomal dominant trait[(85)] . Initially the lesions appear in the childhood and gradually increase in number. The lesions are rounded, skin coloured ,firm papules and nodules of varying sizes, located mainly in the nasolabial folds, nose, forehead cheeks, upper lip and occasionally in the neck scalp and upper trunk. Rarely ulceration and malignant transformation to basal cell carcinoma may occur.

Trichoepithelioma may be associated with Brookes-Spiegle and Rombo syndrome[(88)] systemic lupus erythematosus and myasthenia gravis.

Solitary trichoepithelioma of classical type is more common than multiple variety. It is not inherited and consists of a firm, elevated, flesh colored nodule usually less than 2cms in diameter. Its onset is in childhood or early adult life. Commonly seen over face.

Giant form of this tumour is a rare type that occurs in late life mainly in the thigh and perianal region. Desmoplastic form occurs mostly on the face and

is markedly indurated, clinically it presents with a raised annular border and a depressed centre resembling granulomas annulare. It occurs in adolescence, young adult females[111] .

Histopathology

Consists of mainly two components in the dermis namely the horn cysts and basaloid cells. The former consist of fully keratinized center surrounded by basaloid cells similar to the basal cell carcinoma , but lacking nuclear atypia and frequent mitosis. The keratinisation formed is abrupt and complete and is called as Trichilemmal keratinisation. The tumour islands are composed of basaoloid cells arranged in lace like or adenoid or solid aggregates. They show peripheral pallisading of the cells surrounded by fibrous tissue like stroma .The fibroblasts surrounding the basaloid cells lack the retraction artifact typical of basal cell carcinoma. Sometimes the horn cysts may rupture producing a foreign body granulomatous reaction and calcium deposition may also occur.

The desmoplastic form shows narrow strands of basaloid cells multiple horn cysts and a dense desmoplastic stroma..

Histogeneis

It is assumed that horn cysts represent alteration in hair shaft formation and the basaloid cells surrounding horn cysts are analogous to the hair matrix cells.

Therapy

For Solitary lesions, complete and adequate surgical excision is the best method, followed by the primary closure grafting if necessary .For multiple lesions, plastic repair with cosmetic care is the best mode of therapy. Electro cautery, Cryotherapy and Dermabrasion have also been tried.CO2 laser is also useful.

SEBACEOUS CARCINOMA

It's a rare malignant tumour composed of cells with differentiation towards sebaceous epithelium.

A clinico pathological study of 85 cases adnexal tumours of skin by Reddy Kumaraswamy et al [129 a] showed 17.7 % of incidence of sebaceous carcinoma as compared to the non occurrence of sebaceous carcinoma in north Indian study. It comprises only less than 1 % of all skin tumours. The tumour has been associated with arsenic intake, radio dermatitis and Muir-Torre syndrome. But in our study it occurred in an albinoid skin. Usually the tumour is solitary or multiple covered with normal or verrucous skin .The face and scalp are the commonest site. It is a slowly growing tumour without metastasis. Yellow color of this tumour is a characteristic feature. It may also occur in immuno compromised patients.

Histopathology:

The proportion of cells showing fat globules and degree of cytoplasmic vacoulation are variable. The undifferentiated cells are of moderate size, round in shape with centrally placed nucleus with basophilic cytoplasm and they tend to be grouped in multilobular configurations. The differentiating cells are situated more centrally. Mitotic figures including atypical forms are also seen. Pagetoid infiltration of the epidermis is frequent, when the tumour arises over the eyelids.

Complete excision is the treatment .But nowadays MOHS micrographic surgery is the treatment of choice.

AIMS AND OBJECTIVES OF STUDY

To find out the

1. Overall frequency of surface epidermal and appendageal tumours reported in the out-patient department of dermatology, Government hospital, Chennai.

2. Different clinical presentation such as morphology, site and their associations with other skin and systemic conditions.

3. Histopathological features of various tumours encountered.

MATERIALS AND METHODS

Sixty patients presenting with different forms of epidermal tumours of skin and appendages as their main complaints were selected for the study from the skin department of Government General Hospital, Chennai during the one year period from October 2003 to September 2004 at random. The provisional diagnosis were mainly made by clinical presentations.

The age and sex of all the sixty cases along with their occupation were recorded The duration of the skin lesions in all the patients was also noted. Specific and relevant histories were taken from certain cases with skin tumours and they included history of prolonged intake of any internal medication like inorganic arsenic containing preparation which may lead to basal cell epithelioma.

Family history regarding the presence of tumours was also elicited and it was relevant in trichoepithelioma and steatocystoma multiplex. Menstrual, marital, parturition histories were taken in the female patients. History of medical and surgical intervention for the above complaints if any was also noted in all the sixty patients.

Thorough clinical examination of the skin lesions was carried out in all the cases with special reference to the site, number, size, shape, color, surface, borders, consistency, tenderness and compressibility of the lesions. Whether the lesions were grouped or discrete, sessile, or pedunculated or whether there were any attachment to the underlying structures or the overlying skin were also observed.

Careful General and Systemic examinations were carried out. Investigations like complete haemogram and skin biopsy in the form of both excision and incision biopsy were carried out. The sections for histopathological examination were stained with haematoxylin and eosin and studied in both low and high power magnifications.

In selected cases, X-ray skull, Barium meal study, Barium enema, Upper GI – Endoscopy, ultrasonogram were carried out.

Most of the patients were treated surgically in the form of complete excision of the lesions. Few cases were treated with electrocautery, cryotherapy.

OBSERVATIONS

Of 60 patients studied, 28 were males (46.66 %) and 32 were females (53.33 %). The distribution is given in Chart 2.

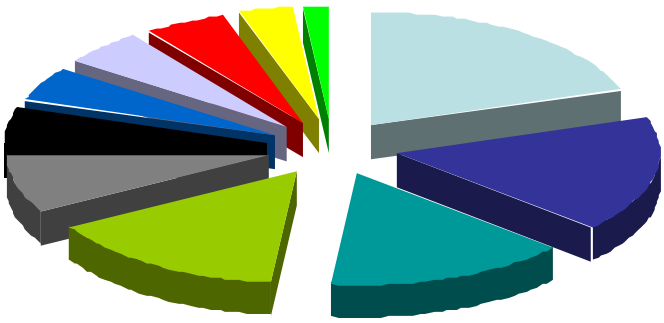
The age and sex distribution is depicted in Table – 1.

AGE AND SEX DISTRIBUTION OF 60 SKIN TUMOURS

TABLE-1

Age group (yrs)	No. of cases		Total	Percentage
	M	**F**		
Birth-1 year	-	-	-	
2-10	3	2	5	8.33
11-20	3	4	7	11.66
21-30	8	6	14	23.33
31-40	3	8	11	18.33
41-50	3	6	9	15.00
51-60	8	6	14	23.33
Total	**28**	**32**	**60**	**100**

DISTRIBUTION OF TUMOURS AS IN 60 PATIENTS



Syringoma = 12

Seborrhoeic keratosis = 10

Epidermal nevus = 9

Epidermal cysts =9

Basal cell carcinoma = 5

Squamous cell carcinoma = 3

Keratoacanthoma =3

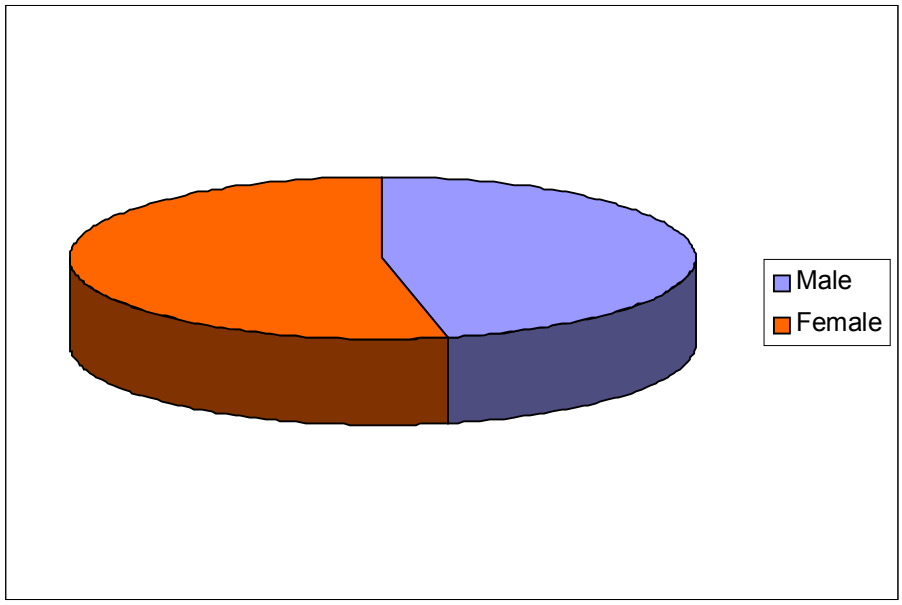
Nevus sebaceous =3

Trichoepithelioma =3

Steatocystoma multiplex =2

Sebaceous carcinoma =1

MALE – FEMALE CASE DISTRIBUTION



MALE = 28 FEMALE = 32

1. SEBORRHOEIC KERATOSIS.

Among ten cases encountered 6 were male patients (60 %) and 4 female patients (40 %).The age and sex distribution in these cases is given in Table-2.Majority of the patients were in their sixth decade.

TABLE-2

AGE AND SEX DISRIBUTION OF 10 CASES OF SEBORRHOEIC KERATOSIS

Age group (yrs)	No. cases		Total	Percentage
	M	F		
10-20	-	-	-	-
21-30	-	-	-	-
31-40	-	-	-	-
41-50	2	2	4	40
51-60	4	2	6	60
Total	**6**	**4**	**10**	**100**

All the cases were asymptomatic except one female who complained of pruritis over the lesions. The lesions appeared as multiple verrucous pigmented papules and plaques of varying sizes covered by scales, stuck on to the skin surface, distributed mainly over the cheeks, temple region and fore head (Fig 1). One female who had pruritis had similar lesions over the chest. She was submitted for investigations to exclude any internal malignancy and that included barium meal, upper GI –endoscopy, ultrasonography and occult blood which proved to be negative.

Excision biopsy of a single lesion was done and histopathology with

haematoxylin & eosin stain showed the classical features of marked hyperkeratosis, irregular acanthosis and papillomatosis (fig. 2) with the presence of pseudo and true horn cysts and basaloid cells. The entire tumour mass was situated above an imaginary line drawn between the two areas of normal looking epidermis on either side.

2. EPIDERMAL NEVUS.

Eight cases of verrucous epidermal nevus and one case of linear epidermal nevus were observed during the study of which 4 were male patients(44.4 %) and 5 female patients (55.5 %). Among them the lesions were present since birth, in 2 male and one female case as in the Table-3.

TABLE - 3

AGE AND SEX DISTRIBUTION OF 9 CASES OF EPIDERMAL NEVUS

Age group (yrs)	No. cases		Total	Percentage
	M	F		
birth-10	3	1	4	44.44
11-20	1	2	3	33.33
21-30	-	2	2	22.22
31-40	-	-	-	-
41-50	-	-	-	-
Total	**4**	**5**	**9**	**100**

Clinically, the lesions were seen as closely set, keratotic, pigmented verrucous papules in a linear fashion of size 2x1 cms distributed unilaterally over the

face, left side of the forehead and left infra orbital region (fig.3). Incision biopsy was done and histopathology with haematoxylin & eosin stain showed marked hyperkeratosis, irregular acanthosis with elongation of the rete ridges and papillomatosis. (fig.4)

3. EPIDERMAL CYST

Epidermal cysts were encountered in 5 male patients (53.55 %) and 4 female patients (44.44%), as in Table-4

TABLE-4

AGE AND SEX DISTRIBUTION OF 9 CASES OF EPIDERMAL CYSTS

Age group (yrs)	No. cases		Total	Percentage
	M	F		
10-20	2	1	3	33.33
21-30	3	1	4	44.44
31-40	-	2	2	22.22
41-50	-	-	-	-
51-60	-	-	-	-
Total	**5**	**4**	**9**	**100**

The lesions were asymptomatic in all the cases. These lesions appeared as elevated, rounded, firm, intradermal cystic nodules of 1 to 2 cms in diameter with stretched and shiny surface, found mainly over the scalp and neck with punctum in 4 cases (fig.5) the number of cysts ranged from 1 to 3 and were not attached to the underlying structures.

Excision biopsy was done and histopathology with haematoxylin &

eosin stain showed the cyst in the dermis, with cyst wall showing all the layers of true epidermis with lamellated keratin inside the cavity (fig.6).

4. STEATOCYSTOMA MULTIPLEX.

Two adult male patients with steatocystoma multiplex were seen duringthe study period. Clinically, the lesions appeared as numerous, small, smooth, round, soft to firm, yellowish cystic nodules of size varying from 1 to 3 cms in diameter, adherent to the overlying skin and were found predominantly over the chest and neck (fig.7). The lesions, to start with were single and in course of few months, new lesions appeared. On puncturing the cysts, oily fluid was extruded in both the cases. There were no other associated skin lesions in both the patients.

Excision biopsy of single lesion was done and histopathology with hamatoxylin & eosin stain showed intricately folded cyst (fig. 8) in the dermis and numerous sebaceous gland lobules attached to both sides of the cyst wall contents of the cyst were eosinophilic.

5. KERATOACANTHOMA

Two male and one female case were reported. Clinically, presented as dome shaped lesions of size ranging from 1-3 cms in diameter with a central crater. All the three cases were solitary type of keratoacanthomas. Solitary keratoacanthoma seen over the left middle finger (fig.9)

Excision biopsy was done and histopathology with haematoxylin & eosin stain showed central keratin filled crater. The epidermis extended like a

buttress over the side of the crater. Also irregular downward proliferations of the epidermis into the dermis and horn cysts were seen.(fig.10).

6. BASAL CELL EPITHELIOMA (BCE)

Five cases were encountered during the period of study, of which 3 were males (60 %) and 2 were females (40 %). The age and sex distribution in these patients is depicted in the Table- 5.Of these 5 patients 4 had nodulo-ulcerative and one had pigmented type (fig.11). All the patients had the lesions of basal cell carcinoma in the face mainly over the cheeks, nose and the pre-auricular region.

TABLE-5

AGE AND SEX DISTRIBUTION OF 5 CASES OF BASAL CELL CARCINOMA

Age group (yrs)	No. cases		Total	Percentage
	M	F		
10-20	-	-	-	-
21-30	-	-	-	-
31-40	-	-	-	-
41-50	1	1	2	40
51-60	2	1	3	60
Total	**3**	**2**	**5**	**100**

Biopsy was done and histopathology with haematoxylin & eosin stain showed tumour masses of basaloid cells and horn cysts with peripheral pallisading and clefts around the islands of basalioma cells with peritumoural lacuna(fig.12).

All the patients were advised surgical intervention with complete excision followed by cosmetic reconstruction in the plastic surgery department. The patients were followed up only for a short period of time (2- 6) months during the study and were advised further follow up every 6 months- 1 year.

7. SQUAMOUS CELL CARCINOMA

One male and two female cases were reported during the study. Sites involved were lower lip, oral mucosa and one case was associated with xeroderma pigmentosum (fig.13,14 and 17) .Incision biopsy of the lesion was done and histopathology with haematoxylin & eosin stain showed massive hyperplasia and horn pearls (fig.15 and 16).

8. SYRINGOMA

Twelve cases of syringoma were observed. All were adults and among them only two were male (16.66 %). The age and sex distribution of syringoma is shown in Table -6.

TABLE-6

AGE AND SEX DISTRIBUTION OF 12 CASES OF SYRINGOMA

Age group (yrs)	No. cases		Total	Percentage
	M	F		
10-20	-	1	1	8.3
21-30	-	3	3	25
31-40	2	4	6	50
41-50	-	1	1	8.3
51-60	-	1	1	8.3
Total	**2**	**10**	**12**	**100**

The syringoma lesions were skin colored, firm, elevated, flat-topped papules of size ranging from 1 to 5 mms in diameter with angular outline and were distributed mainly over the face (fig.18) especially below the lower eyelids. In one adult female, the lesions were also seen in the neck, in addition to face. All the patients sought medical help only for cosmetic disability.

Excision biopsy of a single lesion was done and histopathology withhaematoxylin & eosin stain showed numerous small cystic ductal structures lined by 2 rows of flattened epithelial cells, embedded in dermal fibrous stroma. Some of the ducts also had tail like projections of epithelial stands into the stroma giving a tadpole appearance (fig.19).

9. NEVUS SEBACEOUS OF JADASSOHN

Three adult patients reported with these lesions of whom, 2 were males

and 1 female.

The lesions in all the 3 patients were present since birth but as smaller and flat ones. The patients also gave history of increase in the size of the lesions with verrucous excrescences since adolescence. Clinically they were seen as circumscribed, hyperkeratotic, thickened, verrucous, plaque of size varying from 2 to 4 cms in diameter and were distributed over the parietal and fronto-pareital region of the scalp (fig.20).No other associated eye, skeletal and nervous system involvement.

Excision biopsy was done and histopathology with haematoxylin& eosinstaining showed marked hyperkeratosis, irregular acanthosis, papillomatosis, numerous mature sebaceous glands seen in the upper dermis(fig.21).

The lesions in all the cases were excised with good cosmetic results.

10. TRICHOEPITHELIOMA

Three cases of trichoepithelioma were encountered. All were adults. Of whom 2 were male and 1 female.

The lesions were seen as raised, rounded, skin colored, firm papules and nodules of size varying from 2 to 8 mms in diameter, with few showing telengiectasia over the surface. They were located on the face especially over the paranasal areas, forehead and cheeks (fig. 22).One of these patients underwent plastic surgical repair with good cosmetically results. All the patients reported only for cosmetic disability.

Excision biopsy of a lesion was done and histopathology with haematoxylin & eosin stain showed multiple horn cysts and islands of basoloid or basalioma cells as in the figure 23, which lack high grade, atypia and mitotic activity.

Cosmetic surgical repair is the best mode of therapy.

11. SEBACEOUS CARCINOMA

Only one case of sebaceous carcinoma in an albiniod female was reported in our study. The tumour has been reported in patients with arsenical intake and following radio-dermatitis and in Muir-Torre syndrome. No such associations was seen in our case.

Clinically the lesion started as a plaque (fig.24) before plastic repair gradually increased in size, then it ulcerated. Initially we thought of basal cell carcinoma but the histopathology showed the undifferentiated cells with the centrally placed nuclei and they were grouped in a multi lobular configuration. The differentiated cells were placed centrally. Mitotic activity was seen. It was consistent with sebaceous carcinoma (fig.26 and 27).

Patient was referred to plastic surgery and excision repair was done.

DISCUSSION

The incidence of patients with skin tumours reporting to the dermatology department is becoming more frequent in day-to-day practice. The study included only those patients who were complaining of their skin lesions .Almost all these sixty patients in our study sought medical help mainly for cosmetic reasons.

Of these 60 patients selected for the study, females outnumbered the males.

SEBORRHOEIC KERATOSIS

Seborrhoeic wart was the second common tumour (16.66 %) in our study.

Study of Yeatman JM et al on the prevalence of seborrheoic keratosis in an Australian population reported the frequency of seborrhoeic keratosis in 100 patients in which the prevalence of seborrheoic keratosis was 12 % in 15-25 year old and 100 % in the age group over 50 years [10] . In this study also all the cases were reported above 50 years of age. Cosmetic disfigurement was the main complaint in all the cases. One elderly female who had multiple seborrhoeic keratosis with pruritis was evaluated for possibility of Leser- trelat sign but it did not reveal any internal malignancy. The lesions of seborrhoeic wart were classical in their morphology, distribution and histopathology in all the cases. Electrocautery was considered as the choice of therapy.

EPIDERMAL NEVUS

15 % of the study cases (60) had epidermal nevus. The age of occurrence was at birth or little later as seen in these patients. These lesions were classical in their morphology, distribution and histology in all the patients. A study conducted by Vidaurida la Cruz H et al, reported 7.9 % of epidermal nevus syndrome in 443 patients with epidermal nevi [25a].But in this study one case of epidermal nevus syndrome was reported out of nine cases of epidermal nevus.

One patient showed systemic associations like seizures and visual disturbances. The adult patients were encouraged to undergo surgical excision, which the best mode of therapy.

EPIDERMAL CYST

Epidermal cysts were 15 % in our study cases (60). A clinico pathological study conducted by ChandrasekaranV et al reported that 34 epidermal cysts had punctum in 40 % of the cases. In this study punctum was seen in 44 % of the cases [56a.] All these patients were asymptomatic excepting the cosmetic impairment. The lesions were classical in their morphology and histology. Cosmetically a good response was observed in all the cases following complete excision of the cysts.

STEATOCYSTOMA MULTIPLEX

The incidence of steatocystoma multiplex was 3.33 % in our study cases (60). Even though this disorder is dominantly inherited, our patients did not give family history as in the study conducted by Cha.s et al at Asian medical

centre ,Seoul, Korea which reported most of the cases were sporadic[128]. The lesions were classical in their morphology, distribution, and histopathology in all the cases. Puncturing the lesions extruded oily fluid which helped to diagnose the condition clinically. There were no associated skin lesions like lichen planus, pachyonchia congenita in these cases [73].

KERATOACANTHOMA

These were sixth in order (5 %) in our study cases (60). No precipitating factors Like contact with tar and mineral oil was associated. All these were solitary lesions. All these were classical in their morphology, distribution and histopathology.

None of these developed into malignancy in the follow-up. One case of keratoacanthoma occurred over the site of previous trauma over the left index finger as in the study conducted by Sean et al in which two case were reported in the sites of previous trauma [42 a].

Excision biopsy was advised for these cases to rule out squamous cell carcinoma.

BASAL CELL EPITHELIOMA (BCE)

Five cases of basal cell carcinoma (8.33 %) were reported in our study cases (60).Almost all the patients were asymptomatic except for their cosmetic disability.

Prolonged exposure to sunlight could be the cause for the tumour in 2 of the patients who were manual laborers, with prolonged sun exposure. A study

conducted by Christensen LJ et al at Dept of Dermatology, Mayo clinic, Rochester reported that nodular basal cell carcinoma was the most common subtype [100a] .In this study also nodular basal cell carcinoma was the common type. The adult onset, clinical features and histopathology coincided with the literature reports. None of the other types of basal cell carcinoma like superficial, fibrosing, Fibroepithelioma types were encountered.

A good response was observed in all these patients who were motivated to undergo surgical excision considering the local invasive nature of the tumour.

SQUAMOUS CELL CARCINOMA

In a study conducted by Nuzhat Yasmmen et al, listed 30 squamous cellcarcinoma among the 75 cases studied (40 %) [125a].But in our study (60 cases) squamous cell carcinoma were sixth in order in our study (5 %). One of case was associated with xeroderma pigmentosum as shown in the. In one case squamous cell carcinoma in 21year old was associated with physical growth retardation and hypogonadism. The intelligence was normal. In that case squamous cell carcinoma presented in the left angle of the mouth involving the mucosa. Clinically it presented as ulcers and histopathology was consistent with squamous cell carcinoma.

SYRINGOMA

Majority of the cases (20 %) in the study (60 cases) were having syringoma and this is considered as the commonest tumour encountered in the study. None of these patients had familial predisposition.. Most of these

patients were in the adult age group and were females (83.33 %) as reported. A study conducted by Patrizi et al review of 29 cases of syringoma of which 18 cases were eruptive syringoma but in our study no cases of eruptive syringoma was reported [94a]. The lesions were classical in their morphology, distribution and histology in all the 12 cases. No other special types such as eruptive or chondroid syringoma were encountered.

NEVUS SEBACEOUS

The incidence of nevus sebaceous was 5 % in our study (60 cases). Clinico pathological study of nevus sebaceous of 104 cases by Chang Geng et al, reported most of the cases developed before 10 years (83 %) as apposed to all the cases presented at birth in this study [80a.]. The lesions were classical in their morphology, distribution and histology in all the cases. None of the patients had any systemic associations like skeletal or neurological defects as a part of neurocutaneous syndrome or malignant transformation in the lesions was noted.

Cosmetically acceptable surgical removal was carried out in all the cases .In general, all the patients with these lesions are better encouraged to undergo wide excision of these lesions, even at the early age to prevent the rapid progression of lesions at puberty and possible malignant transformation.

TRICHOEPITHELIOMA

Three cases (5 %) were reported in our study (60 cases). Cosmeticallytrichoepithelioma were more disfiguring than syringoma. The familial occurrences in 50 % of the patients also prompted us for giving genetic

counseling for them.

In the study conducted by Ziprkowski, L et al which also reported familial occurrence in 50 % of the patients [85a]. The lesions in all the cases were classical in their morphology, distribution and histopathology. Neither the special types such as giant or desmoplastic nor ulcerative and malignant transformation were encountered in any of the cases.

SEBACEOUS CARCINOMA

A clinico pathological study of 85 cases of adnexal tumours of skin from South India conducted by Reddy Kumaraswamy, M Et al [129] reported the incidence of 17.7 % of sebaceous carcinoma as against 1.66 % of seborrhoeic carcinoma in this study (60 cases). It presented as a plaque in an albinoid female in the right cheek and later it ulcerated over the face which is common site for this tumour and with characteristic histopathology.

This patient was motivated for plastic surgery for excision.

CONCLUSIONS

- Majority of the patients reported with the skin tumours of epidermis and appendages were adults (83.44 %). The tumours such as epidermal nevus, nevus sebaceous occur in childhood (16.66 %) and these need awareness among the parents to bring the children at an early age. Most of the skin tumours in this study occurred in the age group of 21-30 years and 51-60 years (23.33 %).

- The reporting of the skin tumours was more by the females (53.33 %) compared to males (46.66 %) probably because of their cosmetic awareness.

- The commonest tumour encountered in this study was syringoma (20 %) which were mainly in the infraorbital region and with classical histopathology.

- The second common tumour was seborrheoic keratosis (16.66 %). All the patients had there lesions in the sun exposed areas except one female who had multiple lesions and having classical histopathology.

- Epidermal nevus and epidermal cysts (15%) were the third most common tumour in this study. One case of epidermal nevus was associated with seizures and visual disturbances.

- Basal cell carcinoma (8.33%), squamous cell carcinoma (5%), trichoepithelioma (5%), keratoacanthoma (5%),steatocystoma multiplex(3.33%), nevus sebaceous (5 %), sebaceous carcinoma

(1.66%) were also encountered in our study with classical clinical and histo- pathological findings.

- Rare case like with xeroderma pigmentosum with squamous cell carcinoma was encountered in a male patient.

- One case of squamous cell carcinoma associated with growth retardation and hypogonadism was recorded in this study.

- One case of sebaceous carcinoma of the right cheek was encountered in an albinoid female with characteristic histopathology.

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PROFORMA

Name : **Sex : M / F** **Age :**

Case no : **Hospital no :**

Address : **Occupation** :

Presenting complaints :

Skin lesions

Site

Duration of complaints

Others

Symptoms : pain / burning sensation / itching / cosmetic

Fear of malignancy / discharge / others

Previous treatment : medical / surgical / radiotherapy / others

Consanguineous / Non-Consanguinous

Family history : yes / no

Excessive sun exposure : yes / no

General examination :

Systemic examination :

Dermatological examination :

Primary lesion : macule /papule /patch /nodule /others

Site of the lesion :

Number :single /2-10 /11-20 / >20

Size :

Shape :

Discrete :

Extension :

Pigmentation :

Erythema :

Linearity :

Surface : flat topped elevated raised

Papillomatosis smooth shiny

Verrucous fungoid indurated

Scaling crusted ulcerated

Nodular telengiectasia

Sessile / pedunculated :

Border / margin :

Warmth :

Tenderness :

Bleeds on touch :

Consistency :

Attachment to the underlying structures :

Regional lymph node enlargement :

Any similar lesions :

Other associated findings :

Hair :

Nail :

Mucous membrane :

INVESTIGATIONS

1. Complete blood count

2. Blood group

3. Mantoux

4. VDRL

5. ELISA for HIV

6. SKIN BIOPSY

7. Ultrasound

8. DIAGNOSIS